May 20, 2005

Timothy Adams, Ph.D.
Technical Contact
International Association of Color Manufacturers
HPV Committee
1620 I Street, N.W.
Suite 925
Washington, DC 20006

Dear Dr. Adams:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for C.I. Yellow 23 (FD&C Yellow 5) posted on the ChemRTK HPV Challenge Program Web site on March 19, 2004. I commend the International Association of Color Manufacturers HPV Committee for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that the Committee advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Mark Townsend, Acting Chief of the HPV Chemicals Branch, at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: M. E. Weber
J. Willis

EPA Comments on Chemical RTK HPV Challenge Submission:
C.I. Acid Yellow 23

Summary of EPA Comments

The sponsor, the International Association of Color Manufacturers (IACM), submitted a test plan and robust summaries to EPA for C.I. Acid Yellow 23 (4,5-dihydro-5-oxo-1-(4-sulfophenyl)-4-[(4-sulfophenyl)azo]-1H-pyrazole-3-carboxylic acid trisodium salt; FD&C Yellow No. 5; Tartrazine; CAS No. 1934-21-0) dated March 10, 2004. EPA posted the submission on the ChemRTK HPV Challenge Web site on March 19, 2004. Information is also provided for the proposed analogs FD&C Red No. 40, C.I. Acid Red No. 14, stilbene sulfonic acid derivatives, and FD&C Yellow No. 6 (CAS Numbers were not provided).

EPA has reviewed this submission and has reached the following conclusions:

1. Analog Justification. EPA disagrees with the submitter's proposal to use other azo dyes and stilbene sulfonic acid derivatives as representative compounds for the sponsored chemical.

2. Physicochemical Properties. The data submitted for these endpoints are adequate for the purposes of the HPV Challenge Program.

3. Environmental Fate. The submitter needs to provide measured ready biodegradation data on the sponsored chemical, include a technical discussion on stability in water in the robust summary, and provide the input values for the Level III fugacity robust summary.

4. Health Effects. Adequate data are available for genetic, reproductive and developmental toxicity endpoints for the purposes of the HPV Challenge Program. EPA considers acute and repeated-dose toxicity endpoints adequate on a weight-of-evidence basis. The submitter needs to address deficiencies in the robust summaries.

5. Ecological Effects. These endpoints have not been addressed adequately for the purposes of the HPV Challenge Program; the submitter needs to provide data for all endpoints on the sponsored chemical.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the C.I. Acid Yellow 23 Challenge Submission

Analog Justification

The test plan provided analog data to address or support the direct photodegradation, biodegradation, aquatic toxicity, and *in vivo* genetic toxicity endpoints; however, it did not provide any rationale supporting these analogs.

EPA disagrees with the submitter that the analogs proposed for the ecological effects and biodegradation endpoints are appropriate analogs for the sponsored chemical. In all the proposed analogs a distinguishing feature of the sponsored substance, the azo-linked trisubstituted pyrazole, is conspicuously absent. The proposed biodegradation endpoint analog also contains naphthyl and hydroxynaphthyl groups. The stilbene sulfonic acid derivatives proposed to supply data for the acute fish and invertebrate toxicity endpoints not only lack the azo and pyrazole functions but contain amino or nitro substituents.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, water solubility, and partition coefficient)

The data provided by the submitter for these endpoints are adequate for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The AOPWIN data for photodegradation are adequate for the purposes of the HPV Challenge Program.

Stability in water. While EPA agrees that C.I. Acid Yellow 23 does not contain water-sensitive functional groups, the submitter needs to add a brief technical discussion of this point to the robust summary.

Biodegradation. The biodegradation data are not adequate for the purposes of the HPV Challenge Program. The BIOWIN-estimated data are not an adequate substitute for measured data. The facts do not sustain the submitter's argument–based on data from a non-standard (only 24-hr) test on proposed analog Acid Red 14–that the test substance will not biodegrade because it does not adsorb to sludge. Although Acid Red 14 does not biodegrade under the conditions of the test, several other structurally related dyes mentioned in Shaul *et al.* 1991 are readily biodegradable but do not appear to adsorb to sludge under similar test conditions. Measured ready biodegradation data (OECD TG 301) on the sponsored chemical are needed to address this endpoint.

Fugacity. The submitter needs to provide the input values for parameters used in the Level III estimation in the robust summaries.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available for the genetic, reproductive and developmental toxicity endpoints for the purposes of the HPV Challenge Program. EPA considers acute and repeated-dose toxicity data adequate on a weight-of-evidence basis. The submitter needs to address deficiencies in the robust summaries.

Acute toxicity. Although limited data are available for this endpoint, the overall weight of evidence indicates that this endpoint has been addressed for the purposes of the HPV Challenge Program.

Repeated-dose toxicity. Data were submitted for chronic toxicity/carcinogenicity studies in rats and mice. EPA believes that on a weight-of-evidence basis this endpoint has been addressed for the purposes of the HPV Challenge Program. The submitter needs to provide appropriate robust summaries for this endpoint.

Ecological Effects (fish, invertebrates, and algae)

Acute toxicity to fish, invertebrates, and *algae*. The submitter provided aquatic toxicity data only for chemicals that, as stated above, are not adequately similar to the sponsored chemical, or are incompletely identified (algal test). The ECOSAR values for the sponsored chemical are not appropriate because the ECOSAR model does not yet include a calculation for anionic dyes. Therefore, all three acute aquatic toxicity tests following OECD Test Guidelines are needed on the sponsored chemical.

The references provided for acute fish and invertebrate toxicity in the test plan text (Greim et al, 1994) do not match those in the robust summaries. In addition, the last structure in Table 3 of the test plan does not match the name provided, 2,2'-(1,2-ethenediyl)bis(5-aminobenzenesulfonic acid), dipotassium salt (the molecular structure shows nitro substituents while the name specifies amino groups).

Specific Comments on the Robust Summaries

Health Effects

Repeated-dose toxicity. The submitter needs to prepare a separate robust summary for this endpoint extracting pertinent information, for the 13-week exposure duration, from the 113-week chronic toxicity/carcinogenicity studies: for example, general study information, method description, and effects on body weight, food consumption, clinical pathology findings, necropsy and histopathological findings at the earliest sacrifice interval (in this case, 1 year), NOAEL and LOAEL values etc.

Genetic toxicity. *Gene mutations.* Information missing from the Ames test (Chung et. al., 1981) included culture conditions (e.g., temperature and medium used), duration of incubation, number of colonies counted per concentration, the source of the metabolic activation system, responses of positive control substances, whether or not testing was conducted both with and without metabolic activation and the results for each of these test conditions.

Chromosomal aberrations. Information missing from the *in vitro* chromosomal aberrations study included culture conditions (e.g., incubation temperature), actual test concentrations, and use and response of positive control substances.

Reproductive toxicity. The robust summary for a lifetime toxicity/carcinogenicity dietary study in rats did not report pup body weight data, sex ratio of pups, estrus cycle and sperm parameters.

Developmental toxicity. Information missing from the study in rats included the proportions of fetuses examined for external, skeletal and visceral malformations, and the sex of fetuses.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.